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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,531	06/17/2005	Mark E Fraley	21272YP	6761
210	7590	08/19/2008	EXAMINER	
MERCK AND CO., INC			ROBINSON, BINTA M	
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RAHWAY, NJ 07065-0907			ART UNIT	PAPER NUMBER
			1625	
			MAIL DATE	DELIVERY MODE
			08/19/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/539,531	FRALEY ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	BINTA M. ROBINSON	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_.
- 2a) This action is **FINAL**.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-20 is/are pending in the application.
  - 4a) Of the above claim(s) 10 and 16-20 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_ is/are allowed.
- 6) Claim(s) 1-9, 11-15 is/are rejected.
- 7) Claim(s) \_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. ____ .
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>1/26/06</u> .	6) <input type="checkbox"/> Other: ____ .

**Detailed Action**

***Election/Restrictions***

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-9, 11-15, drawn to compounds, compositions and a method of making them.

Group II, claim(s) 10, 16-20, drawn to various uses of the compound.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups I and II are linked by the technical feature of compound I. However, as evidenced by Hcaplus 112:97889, compound I does not make a contribution over the prior art and does not link the product and method claims into a single general inventive concept. If applicants elect the product and if it is found free of the prior art, the method claims may be eligible for rejoinder practice under 821.04(b).

2. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

The species in claim 6, 7, and 8

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims

subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic: 1-5, 9-18.

3. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The species lack a common core. During a telephone conversation with Attorney Nicole Beeler on 3/12/08 and on 6/23/08, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-9, 11-15 and the species in claim 8 was elected.

Affirmation of this election must be made by applicant in replying to this Office action.

Claims 10, 16-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 9, 11, 12, 13 14-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 10, 12-16 of copending Application No. 10539512. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application teaches a genus of compounds and compositions which overlap substantially in subject matter with the instant genus of compounds and compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The copending application teaches the instant compound as shown in Formula I, at claim 1 and compositions containing them. The difference between the prior art compound and compositions and the instantly claimed compounds and composition is

Art Unit: 1625

the teaching of a generic compound which overlaps in subject matter with the instant genus of compounds. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds and compositions. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds and compositions.

1. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

2. Claims 6 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 6 of copending Application No. 10539512. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Both claims claim the instant compound, 1-acetyl-4-(2,5-difluorophenyl)-6-phenyl-1,2,3, 6-tetrahydropyridine.

### **Paragraph 8.28**

Claims 1-5, 9, 11, 12, 13 14-15 are directed to an invention not patentably distinct from claims 1-5, 10, 12-16 of commonly assigned 10539512. Specifically, Claims 1-5, 9, 11, 12, 13 14-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 10, 12-16 of

copending Application No. 10539512. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application teaches a genus of compounds and compositions which overlap substantially in subject matter with the instant genus of compounds and compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The copending application teaches the instant compound as shown in Formula I, at claim 1 and compositions containing them. The difference between the prior art compound and compositions and the instantly claimed compounds and composition is the teaching of a generic compound which overlaps in subject matter with the instant genus of compounds. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds and compositions. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds and compositions.

.The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending application 10593512, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can,

Art Unit: 1625

under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

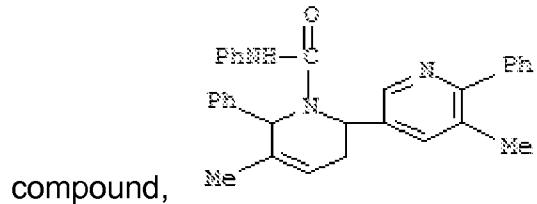
A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 1, 9, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Hcaplus 112:97889. (See Reference U). Hcaplus 112:97889 discloses the instant



The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

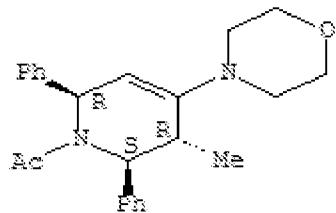
A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10, 12, 13, and 14 are rejected under 35 U.S.C. 102(b) as being

anticipated by Hcaplus 1999:287417. Hcaplus 1999:287417 discloses the

instant compound



. This compound anticipates the instant claims, because R1 is moiety #1 wherein n is 0, and X is oxygen, R9 is hydrogen, and R2 is hydrogen, and R3 is #12 wherein r is 0, s is 0, C0-C6 alkylene has a value of 0 and aryl is phenyl, R4 and R5 are hydrogen, R6 is heterocyclyl which is morpholine and, R8 is aryl which is phenyl and R9 is hydrogen.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 10, 12, 13, 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I with R1 equal to substituted carbonyl moiety as claimed, R6 equal to phenyl optionally substituted as claimed, R9 equal to hydrogen or -(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub>, R8 equal to phenyl optionally substituted as claimed, does not reasonably provide enablement for using the compounds of formula I with, R1, R6, R8, R9 equal to all other moieties claimed. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope

with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds with radicals R1, R6, R8 and R9 would be active would require synthesis of the substrate and subjecting it to testing with Applicants' immunofluorescence microscopic assays, cell proliferation assays, mitotic arrest and apoptosis by FACS assay, protein purification assay, and Kinesin ATPase In vitro assay. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found at page 46, lines 20-25 which merely states Applicants' intent to make and use such compounds. c) In the instant case, none of the working examples contains any radicals R1, R6, R8 and R9 equal to the moieties claimed other than those stated to be enabled above. d) The nature of the invention is inhibition of mitotic kinesins and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the mitotic kinesins, the binding activity of small ligands to that mitotic kinesins, and the ability of those compounds to inhibit mitotic kinesins. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of such

diverse rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. The diverse claimed compounds are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). *In re Fouche*, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) *In re CAVALLITO AND GRAY*, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had equal hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic

structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various heterocyclic radicals, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/

Examiner, Art Unit 1625

Application/Control Number: 10/539,531  
Art Unit: 1625

Page 13

/JANET L. ANDRES/

Supervisory Patent Examiner, Art Unit 1625